

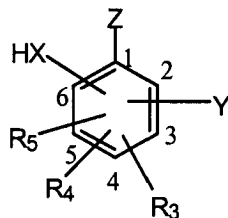
1. CLAIM AMENDMENTS (LISTING OF CLAIMS)

*This listing of claims will replace all prior versions and listings of claims in the application:*

1. (Currently Amended) A method of

- a) synthesis of a linear or cyclic peptide;
- b) synthesis of a C-terminal modified peptide; or
- c) on-resin cyclization of a peptide molecule,

said method comprising at least the step of linking a cyclic aromatic auxiliary compound of General Formula II to a primary amine nitrogen atom of an amino acid, or of a peptide which is to be cyclized or modified, to form a secondary amine



in which

~~X is oxygen, sulfur, CH<sub>2</sub>O, or CH<sub>2</sub>S;~~

**XH** is OH, SH, CH<sub>2</sub>OH, or CH<sub>2</sub>SH;

**Y** is an electron-withdrawing group;

**Z** is any group which allows the formation of a covalent carbon-nitrogen bond;  
and

**R<sup>3</sup>**, **R<sup>4</sup>** and **R<sup>5</sup>** are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl aryloxy, **XH** or **Y**, or a covalent linkage to a solid support; and

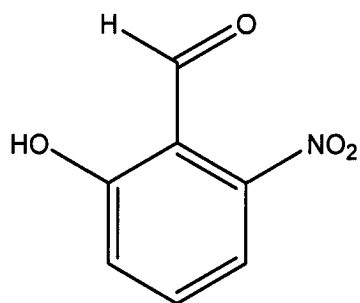
in which **R<sup>3</sup>** and **R<sup>4</sup>**, or **R<sup>4</sup>** and **R<sup>5</sup>** can optionally together with the ring form a 5-, 6-, or 7-membered ring, thereby to facilitate conversion of the secondary amine to an amide, activating the carboxylic acid group of the amino acid, or of a peptide which is to be cyclized or modified, and converting the secondary amine to an amide.

2. (Previously Presented) The method of claim 1, in which **Y** is nitro, ketone, carboxylic ester, amide, nitrile, sulfonamide, sulfoxide, sulfone, sulfonate, fluoride, chloride, bromide or iodide.

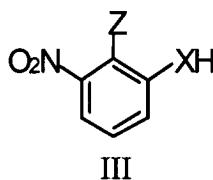
3. (Previously Presented) The method of claim 1, in which **Z** is an aldehyde, alkylalcohol, alkylhalide, or a ketone, or is a halogenated C<sub>1-3</sub> alkyl group.
4. (Previously Presented) The method of claim 3, in which the halogenated alkyl group is a halogenated methyl group.
5. (Previously Presented) The method of claim 4, in which the halogen is iodine, bromine or chlorine.
6. (Canceled)
7. (Previously Presented) The method of claim 1, in which the **XH** group is at position 2 or 3 in General Formula II, and **Y** is at any other position.
8. (Previously Presented) The method of claim 7, in which the **XH** group is at position 2.
9. (Previously Presented) The method of claim 7, in which **Y** is at position 6.

10. (Previously Presented) The method of claim 9, in which Y is NO<sub>2</sub>.

11. (Previously Presented) The method of claim 1, in which the auxiliary compound is

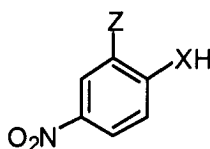


12. (Previously Presented) The method of claim 1, for synthesis of a cyclic peptide, a large peptide, or a difficult peptide, in which the auxiliary compound is of General Formula III



and the auxiliary compound is removed by photolysis following amide bond formation.

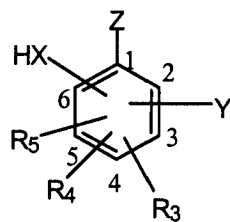
13. (Previously Presented) The method of claim 1, for synthesis of a cyclic peptide, a large peptide, or a difficult peptide containing one or more substituted amide bonds, in which the auxiliary compound is not removed, and the auxiliary compound is of General Formula IV



IV

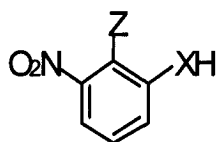
14. (Currently Amended) A method of
- a) synthesis of a compound selected from the group consisting of linear and cyclic peptides, large peptides with a native peptide backbone, and “difficult” peptide sequences,
  - b) backbone linkage for the synthesis of peptides, C-terminal modified peptides, or
  - c) on-resin cyclization,

said method comprising at least the steps of: linking a cyclic auxiliary compound of General Formula II,



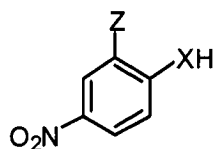
II

General Formula III,



III

or General Formula IV



IV

in which

~~X is oxygen, sulfur, CH<sub>2</sub>O, or CH<sub>2</sub>S;~~

XH is OH, SH, CH<sub>2</sub>OH, or CH<sub>2</sub>SH;

Y is an electron-withdrawing group;

**Z** is any group which allows the formation of a covalent carbon-nitrogen bond;  
and

**R<sup>3</sup>**, **R<sup>4</sup>** and **R<sup>5</sup>** are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, alkoxy, aryloxy, XH or Y, or a covalent linkage to a solid support, and

in which **R<sup>3</sup>** and **R<sup>4</sup>**, or **R<sup>4</sup>** and **R<sup>5</sup>** can optionally together with the ring form a 5-, 6-, or 7-membered ring

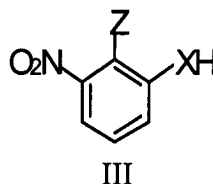
to a primary amine nitrogen atom of a starting peptide molecule, to form a secondary amine, thereby to facilitate conversion of the amine to an amide activating the C-terminal carboxylic acid group of the peptide, and converting the secondary amine to an amide.

15. (Previously Presented) The method of claim 14, in which **XH** in General Formula II is at position 2, and **Y** is NO<sub>2</sub> at position 6.

16. (Previously Presented) The method of claim 1, in which  $R^3$ ,  $R^4$ , and  $R^5$  are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, and a covalent linkage to a solid support.
17. (Previously Presented) A method of synthesis of a cyclic peptide, comprising the steps of
- a) synthesizing a linear peptide to be cyclized,
  - b) linking an auxiliary compound as defined in claim 1 to a selected primary amine of the linear peptide to form a secondary amine, thereby facilitating conversion of the amine to an amide,
  - c) activating a selected carboxylic acid to effect cyclization, and where necessary inducing ring contraction, and optionally
  - d) removing the auxiliary compound after complete N-acylation.
18. (Previously Presented) The method of claim 17, in which ring contraction is induced by heating or by addition of a metal.

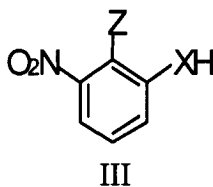


19. (Previously Presented) The method of claim 17, in which the auxiliary compound is of General Formula III,



and the auxiliary compound is removed by photolysis.

20. (Previously Presented) The method of claim 17, in which steps a) to d) are performed on a solid support, and are followed by cleavage of the cyclic product from the solid support.
21. (Previously Presented) The method of claim 17, in which activation of the C-terminal carboxylic acid is performed in the presence of an auxiliary compound of General Formula III,

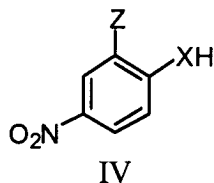


and the cyclization is performed by attaching the auxiliary compound to the selected amine via the Z-group.

22. (Previously Presented) A method of synthesis of a large peptide with a native peptide backbone, comprising the steps of:

- a) synthesizing a set of peptide fragments to be linked to form a large peptide;
- b) linking an auxiliary compound as defined in claim 1 to the primary amine of the first peptide fragment to form a secondary amine, thereby facilitating conversion of the amine to an amide;
- c) activating the C-terminal carboxylic acid of the second peptide fragment;
- d) adding the second peptide fragment to the first peptide fragment and forming a peptide bond between the two fragments; and optionally
- e) removing the auxiliary compound after N-acylation is complete.

23. (Currently Amended) The method of claim 21, [[in which the auxiliary compound is of General Formula IV,

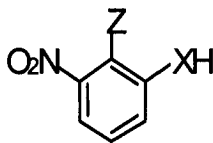


and]]wherein the auxiliary compound is removed by photolysis.

24. (Previously Presented) A method of synthesis of a difficult peptide sequence, comprising the steps of:

- a) linking an auxiliary compound as defined in claim 1 to one or more  $\alpha$ -nitrogen atoms of amino acids in a starting peptide which is linked to a solid support;
- b) synthesizing the complete difficult peptide using standard solid phase synthesis methods; and optionally
- c) when synthesis is complete, removing the auxiliary compound.

25. (Previously Presented) The method of claim 24, in which the auxiliary compound is of General Formula III,



III

and the auxiliary compound is removed by photolysis.

26. (Previously Presented) A method of backbone linkage for synthesis of a linear peptide, comprising the steps of:
- a) using an auxiliary compound as defined in claim 1 as a linker linking the  $\alpha$ -nitrogen of an amino acid residue in the selected peptide to a solid support to form a secondary amine, thereby to facilitate conversion of the amine to an amide;
  - b) assembling the linear peptide using standard solid phase peptide synthesis methods; and optionally
  - c) removing the side chain protecting group(s); and/or

- d) cleaving the peptide from the solid support.
- 
- 27. (Previously Presented) The method of claim 26, in which the C-terminal amino acid residue of the selected peptide is a modified amino acid in which the carboxyl group is replaced by a functional group.
  - 28. (Previously Presented) The method of claim 27, in which the functional group is an ester, alkylalcohol, acetal, or amide group.
  - 29. (Previously Presented) The method of claim 26, in which Y is nitro in position 6, **XH** is in position 2, and cleavage is performed by photolysis.
  - 30. (Previously Presented) A method of on-resin cyclization of a linear peptide, comprising the steps of:
    - a) using an auxiliary compound as defined in claim 1 as a linker linking the  $\alpha$ -nitrogen of an amino acid residue in the desired peptide to a solid

support to form a secondary amine, thereby to facilitate conversion of the amine to an amide,

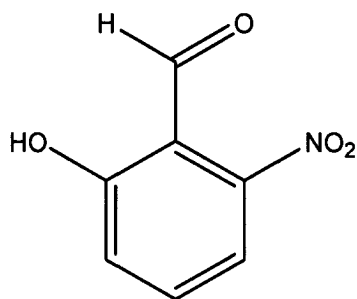
- b) synthesizing a linear peptide on a solid support, using standard solid phase peptide synthesis methods,
- c) deprotecting the desired amine and carboxylic acid groups;
- d) activating the carboxylic acid group to perform cyclization; and optionally
- e) deprotecting amino acid side chain groups; and/or
- f) cleaving the cyclic peptide from the solid support.

31. (Previously Presented) The method of claim 30, in which **Y** is a nitro group in position 6, **XH** is in position 2, and cleavage is performed by photolysis.

32.-34. (Canceled)

35. (Previously Presented) The method of claim 15, in which  $R^3$ ,  $R^4$ , and  $R^5$  are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, and a covalent linkage to a solid support.
- 36-38. (Canceled)
39. (Previously Presented) The method of claim 20, in which side-chain protecting groups are removed after cleavage of the cyclic product from the solid support.
40. (Previously Presented) The method of claim 22, in which steps (a) to (e) are repeated to add the remaining members of the set of peptide fragments until the large peptide is complete.
41. (Currently Amended) A method of synthesizing a linear or cyclic peptide, said method comprising at least the steps of:

(i) linking a cyclic aromatic auxiliary compound of the formula:



to a primary amine nitrogen atom of an amino acid or of a peptide which is to be cyclized or modified, to form a secondary amine;

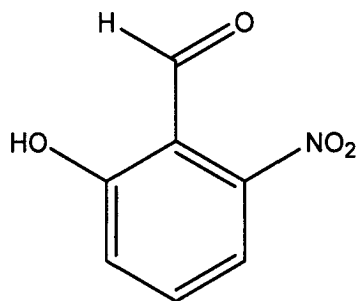
(ii) ~~converting said secondary amine to an amide;~~

~~(iii)~~—activating the carboxylic acid group of said amino acid or said peptide; and

~~(iv)~~(iii) converting the resulting secondary amine to an amide.

42. (Currently Amended) A method of synthesizing a C-terminal modified peptide, said method comprising at least the steps of:

(i) linking a cyclic aromatic auxiliary compound of the formula:



to a primary amine nitrogen atom of an amino acid or of a peptide which is to be cyclized or modified, to form a secondary amine;



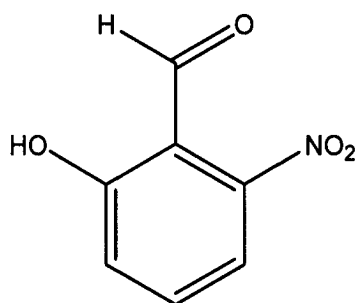
(ii) ~~converting said secondary amine to an amide;~~

(iii) ~~—activating the carboxylic acid group of said amino acid or said peptide; and~~

~~(iv)~~(iii) converting the resulting secondary amine to an amide.

43. (Currently Amended) A method of on-resin cyclization of a peptide or peptidomimetic, said method comprising at least the steps of:

(i) ~~linking~~ using a cyclic aromatic auxiliary compound of the formula:



as a linker linking the  $\alpha$ -nitrogen of an amino acid residue in the desired peptide of peptidomimetic to a solid support to form a secondary amine, thereby to facilitate conversion of the amine to an amide;

(ii) synthesizing a linear peptide or peptidomimetic on a solid support, using standard solid phase peptide synthesis methods;

(iii) deprotecting the desired amine and carboxylic acid groups;

(iv) activating the carboxylic acid group to perform cyclization; and optionally

(v) deprotecting amino acid side chain groups; and/or

(vi) cleaving the cyclic peptide from the solid support.

~~to a primary amine nitrogen atom of an amino acid or of a peptide which is to be~~

~~cyclized or modified, to form a secondary amine;~~

~~(ii) converting said secondary amine to an amide;~~

~~(iii) activating the carboxylic acid group of said amino acid or said~~

~~peptide; and~~

~~(iv) converting the resulting secondary amine to an amide.~~